

Old Claim No.	Previous Status	Proposed New Claim No.
88	allowed	179
89	allowed	183
90	allowed	186
94	allowed	198
117		178
118	allowed	178
119	allowed	178
120	allowed	178
121		178
122		179
123		181
124	allowed	180
126		182-184
127		185-187
128		188, 190
129		188, 190
130		188, 190
131		188, 189
132		188, 189
133		193
134		194
135	allowed	195
137	allowed	182
138	allowed	185
139	allowed	188
140	allowed	188
142	allowed	193
143		197-199
144		204
145		204
146		None

Old Claim No.	Previous Status	Proposed New Claim No.
147		205
148		207
149		197
150	allowed	195
151	allowed	203
152	allowed	202
153		202
154	allowed	204
155	allowed	208
156	allowed	207
157	allowed	206
158	cancel	
159	allowed	195
160	allowed	195
165	allowed	202
166	allowed	202
167	allowed	206
168	allowed	207
169	allowed	None
170	allowed	None
171	allowed	None
172		None
173		None
174		None
175	allowed	189
176	allowed	198
177	allowed	197

Please cancel claims 88-90, 94, 117-135, 137-140, 142-160, 165-177, without prejudice, and replace them with the new claims provided below.

178. A purified and isolated nucleic acid encoding a glial cell line-derived neurotrophic factor (GDNF) polypeptide, wherein said nucleic acid:

- (a) comprises nucleotides 304 through 705 of SEQ ID NO:3; or
- (b) comprises nucleotides 105 through 506 of SEQ ID NO:5; or
- (c) encodes a polypeptide comprising the amino acid sequence set forth as 1-134 of SEQ ID NO:4; or
- (d) encodes a polypeptide comprising the amino acid sequence set forth as 1-134 of SEQ ID NO:6; or
- (e) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding the polypeptide of SEQ ID NO:6 under hybridization conditions comprising 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C and wherein said polypeptide promotes dopamine uptake in dopaminergic neurons; or
- (f) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding amino acids 2 to 86 of SEQ ID NO:4 under hybridization conditions comprising 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C and wherein said polypeptide promotes dopamine uptake in dopaminergic neurons.

179. The nucleic acid of claim 178 wherein said nucleic acid additionally encodes for an amino-terminal methionine residue when said GDNF polypeptide is recombinantly produced by a bacterial expression system.

180. A purified and isolated nucleic acid encoding a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:27 or SEQ ID NO:28.

181. A purified and isolated nucleic acid comprising a nucleic acid fully complementary to the nucleic acid of claim 178, 179, or 180.

182. An expression vector comprising the nucleic acid of claim 178.

183. An expression vector comprising the nucleic acid of claim 179.
184. An expression vector comprising the nucleic acid of claim 180.
185. An isolated host cell comprising the expression vector of claim 182.
186. An isolated host cell comprising the expression vector of claim 183.
187. An isolated host cell comprising the expression vector of claim 184.
188. The host cell of claim 185 wherein said cell is selected from the group consisting of :
 - (a) a microorganism;
 - (b) an animal cell;
 - (c) a COS cell;
 - (d) a bacterial cell; and
 - (e) *E. coli*.
189. The host cell of claim 186 or 187 wherein said cell is selected from the group consisting of :
 - (a) a bacterial cell; and
 - (b) *E. coli*.
190. The host cell of claim 187 wherein said cell is selected from the group consisting of :
 - (a) a microorganism;
 - (b) an animal cell;
 - (c) a COS cell;
 - (d) a bacterial cell; and
 - (e) *E. coli*.
191. The host cell of claim 185 or 187 wherein said cell produces said GDNF polypeptide.

192. The host cell according to claim 191 wherein said cell secretes said GDNF polypeptide.

193. The host cell according to claim 192 wherein said cell is an animal cell transformed or transfected *ex vivo*.

194. The host cell according to claim 193 wherein said cell is suitable for human implantation.

195. An isolated host cell which expresses a nucleic acid encoding a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons, wherein said nucleic acid is operatively linked to a non-native promoter in an expression vector and wherein said nucleic acid:

- (a) comprises nucleotides 304 through 705 of SEQ ID NO:3; or
- (b) comprises nucleotides 105 through 506 of SEQ ID NO:5; or
- (c) encodes a polypeptide comprising the amino acid sequence set forth as 1-134 of SEQ ID NO:4; or

- (d) encodes a polypeptide comprising the amino acid sequence set forth as 1-134 of SEQ ID NO:6; or

- (e) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding the polypeptide of SEQ ID NO:6 under hybridization conditions comprising 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C; or

- (f) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding amino acids 2 to 86 of SEQ ID NO:4 under hybridization conditions comprising 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C.

196. An isolated host cell which expresses a nucleic acid encoding a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons, wherein said nucleic acid is operatively linked to a non-native promoter in an expression vector and wherein said nucleic acid encodes a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:27 or SEQ ID NO:28.

197. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 182 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

198. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 183 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

199. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 184 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

200. The method according to claim 197, 198, or 199 further comprising a step of refolding said GDNF polypeptide.

201. The method according to claim 197, 198, or 199 further comprising a step of refolding said GDNF polypeptide to form a disulfide-bonded dimer.

202. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing the host cell of claim 195 or 196 under conditions suitable for the expression of said GDNF polypeptide; and
- (b) isolating said GDNF polypeptide produced in a substantially purified form from said host cell culture.

203. The method according to claim 202 wherein said nucleic acid further comprises a codon encoding an amino-terminal methionine residue when said GDNF polypeptide is recombinantly produced by a bacterial expression system.

204. The method according to claim 202 wherein said host cell is selected from the group consisting of :

- (a) an animal cell; and
- (b) a COS cell.

205. The method according to claim 203 wherein said host cell is selected from the group consisting of :

- (a) a bacterial cell; and
- (b) *E. coli*.

206. The method according to claim 204 wherein the GDNF polypeptide produced is secreted by said host cell.

207. The method according to claim 205 further comprising a step of refolding the GDNF polypeptide produced to form a dimer.

208. The method according to claim 206 further comprising a step of refolding the GDNF polypeptide produced to form a dimer.

209. The method according to claim 205 further comprising a step of refolding the GDNF polypeptide produced to form a disulfide-bonded dimer.

210. The method according to claim 206 further comprising a step of refolding the GDNF polypeptide produced to form a disulfide-bonded dimer.

REMARKS

Claims 88-90, 94, 118-120, 124, 135, 137-140, 142, 150, 152, 154-157, 160, 165-171, and 175-177 were previously allowed. The claims that were pending in the case were either rewritten in response to the Examiner's objections as to form or canceled (to remove duplicative